IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Szpirer et al.
App. No	:	10/507,923
Filed	:	July 19, 2005
For	:	POISON/ANTIDOTE GENETIC SYSTEMS FOR THE SELECTION OF GENETICALLY MODIFIED EUCARYOTE CELLS OR ORGANISMS
Examiner	:	Kevin Kai Hill
Art Unit	:	1633
Conf #	:	6813

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Jerry L. Hefner, Reg. No. 53,009

PETITION FROM REQUIREMENT FOR RESTRICTION UNDER 37 C.F.R. §1.144

Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Pursuant to 37 C.F.R. § 1.144, Applicants hereby petition the Commissioner to review the Examiner's final decision to maintain the Restriction Requirement as set forth in section 3 of the Office Action issued March 29, 2007.

STATEMENT OF FACTS

On July 19, 2005, Applicants completed the requirement for entering the US national phase for the above-referenced application. The Application was filed with 19 claims (claims 15-33) of which two claims (claims 15 and 29) were independent. On March 29, 2007, the Examiner issued a Restriction Requirement asserting that these 19 claims should be divided into three different groups (see section 1 of the Restriction Requirement). Additionally, in section 3 of the Restriction Requirement, the Examiner required that Applicants elect several specific embodiments of the invention for further prosecution. The Examiner asserted that many of the

embodiments were presented using alternative language, and thus, *a prori* lacked unity of invention. The Examiner also asserted that these embodiments could not be searched and examined together without serious burden. At page 5 of the Restriction Requirement, the Examiner went on to assert that the restriction of subject matter set forth in section 3 should not be construed as an election of species. Finally, the Examiner contended that Applicants' reply must "identify the claims readable on the elected embodiments, including any claims subsequently added" (see Restriction Requirement at page 6).

In response to the Restriction Requirement, Applicants elected claim group I without traverse and made several provisional elections, with traverse, of the other restricted subject matter identified in section 3 of the Restriction Requirement. In particular, Applicants provisionally elected (1) "does not comprise a selectable marker," (2) "wherein the genetic sequence encoding the antidote is not added to the construct," (3) "ccdB," (4) "yeast cell," (5) "an exogenous compound," (6) "chloroplast," and (7) "two different toxic genes," all with traverse. Briefly, and as re-iterated below, Applicants argued that, among other things, that the elected claims include a common special technical feature over the prior art and that the Examiner made no argument as to why such technical feature would not be unifying. Furthermore, Applicants argued that the Examiner did not appropriately apply the rules used for evaluating unity of invention in US national phase applications, but rather, applied, what appeared to be, "a mixture of the rules for restricting independent and distinct subject matter, the USPTO policy related to nucleotide and amino acid sequence searching, and the rules for restriction based on patentably distinct species all weaved together using the vocabulary found in the rules related to unity of invention requirement." Finally, even though Applicants disagreed with the Examiner's contention that embodiments of the invention presented using alternative language *a priori* lack of unity of invention, seven new claims were added in order to separate subject matter that was presented in claims 15-28 using "alternative language."

In the Office Action issued December 12, 2007, the Examiner acknowledged Applicants' election of claim Group I, acknowledged Applicants' provisional elections of specific embodiments of the invention, withdrew each of new claims 34-40 without explanation and made the Restriction Requirement issued March 29, 2007 final. In making the Restriction Requirement final, the Examiner stated that the reference Norris et al. renders Applicants' special

technical feature non-unifying because the reference allegedly discloses "discloses the use of poison/antidote genetic systems in eukaryotic cells." The Examiner then went on to assert that search and examination of each of the restricted embodiments would require a serious burden, and thus, the claimed embodiments could not be searched and examined together (see page 3 of the Office Action issued December 12, 2007).

In view of the foregoing reasoning, the non-elected embodiments as well as the subject matter of claims 34-40 were withdrawn from further consideration as being drawn to a nonelected inventions.

ACTION REQUESTED

Applicants continue to traverse the restriction of "non-elected" embodiments of the invention and request rejoinder of withdrawn dependent claims 34-40.

The claimed invention

The subject matter recited in independent claim 15 of the instant application as filed is set forth as follows:

15. A recombinant eucaryote cell or organism with the proviso that it is not an element selected from the group consisting of a human germ cell line, a human zygote, a human embryo and a human individual, said cell or organism having incorporated in its genome

i) a genetic construct made of incorporated in its genome, said genetic construct comprising at least one nucleotide sequence and optionally a selectable marker, said sequence encoding comprising a toxic gene (TOX) under the control of an inducible promoter/operator genetic sequence, said toxic gene encoding a poison protein selected from a poison/antidote group; and

ii) a genetic sequence (ANTITOX) encoding an antidote molecule to said toxic molecule poison protein with the condition that the sequence encoding the antidote molecule is not present natively in said cell or organism, and wherein the genetic sequence encoding the antidote is added to the construct or is in an episomal DNA introduced in the eucaryote cell or organism.

In response to the Restriction Requirement issued March 29, 2007, independent claim 15 was amended as follows:

15. (Currently amended) A recombinant eucaryote cell or organism with the proviso that it is not an element selected from the group consisting of a human germ cell line, a human zygote, a human embryo and a human individual, said cell or organism having ~~incorporated in its genome~~

i) a genetic construct ~~made of~~ incorporated in its genome, said genetic construct comprising at least one nucleotide sequence ~~and optionally a selectable marker~~, said sequence ~~encoding~~ comprising a toxic gene (TOX) under the control of an inducible promoter/operator genetic sequence, said toxic gene encoding a poison protein selected from a poison/antidote group; and

ii) a genetic sequence (ANTITOX) encoding an antidote molecule to said ~~toxic molecule~~ poison protein with the condition that the sequence encoding the antidote molecule is not present natively in said cell or organism~~, and wherein the genetic sequence encoding the antidote is added to the construct or is in an episomal DNA introduced in the eucaryote cell or organism~~.

Embodiments deleted from amended claim 15 were re-presented individually in dependent claims 34-36. Similarly, embodiments deleted from dependent claims 24, 27 and 28 were individually re-presented in dependent claims 37-40.

The claimed subject matter was not properly restricted

Applicants respectfully submit that the claimed subject matter meets the unity of invention requirements. Furthermore, Applicants submit that there is no basis for restricting embodiments of claims, whether present in the alternative or separate dependent claims, from the generic invention as claimed. Applicants acknowledge that a restriction of species may be required when an Applicant claims numerous species that fall within the scope of a generic linking claim; however, no such restrictions have been presented in this case. Rather, the Examiner seeks to eliminate rightfully included embodiments of Applicants' generic invention from the subject matter that is currently being searched and examined.

Applicants have already presented arguments as to why the restriction of subject matter set forth in the Restriction Requirement issued March 29, 2007 does not comply with the rules for evaluating unity of invention. Applicants believe these arguments to be sufficient to overcome the instant restriction requirement, and therefore, reiterate those arguments below.

Arguments traversing the Restriction Requirement as set forth in Applicants' response filed September 24, 2007

The Examiner alleges that the restriction set forth in section 3 of the Restriction Requirement is proper because certain claims are "directed to more than one biologically distinct organisms and structurally distinct genetic constructs." The Examiner also alleges that elements of claims that are related by conditional or alternative language "are deemed to lack unity of invention *a priori* because they are not so linked as to form a single general inventive concept under PCT Rule 13.1." Applicants do not agree.

The unity of invention requirements under PCT Rule 13.1 is implemented into the Rules of Patent Practice through 37 C.F.R. § 1.475. Section (e) of rule 1.475 plainly states that "the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim." As such, alternative language is not a grounds for establishing lack of unity of invention *a priori*.

In addition to stating that certain claim language causes an *a priori* lack of unity of invention as discussed above, the Examiner goes on to argue the restriction is proper under PCT Rule 13.1 and PCT Rule 13.2. In particular, the Examiner's arguments are set forth as follows:

> The embodiments listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the embodiments lack the same or corresponding special technical features for the following reasons:
>
> The embodiments are drawn to multiple organismal and nucleic acid sequences that are structurally distinct, independent and mutually exclusive embodiment that yields distinctly different effects. The numerous variations in

the number, position and type of nucleic acid sequences and the gene products encoded therein result in a vast genus of structurally unrelated molecules that are not obvious variations of each other. Each of the embodiments confers a unique, non-obvious, distinctly different technical feature onto the transgenic cell or organism that will directly impact toxicity or bioactivity of the gene products and are non-obvious variants because one of ordinary skill in the art would not expect an episomal genetic construct to be equivalent in stability and generational inheritance as a genetic construct that has integrated into the nuclear genome, for example. Similarly, an artisan would not expect ccdB to be identical in effect as Hok proteins. Applicants are reminded that nucleic acid sequences encoding different proteins, and the amino acid sequences they encode, are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitute independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleic acid and amino acid sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 C.F.R. 1.141 et seq. Similarly, each transgenic organism is considered a distinct invention.

Given the breadth of the claimed, unrelated structures, a search for all possible embodiments imposes an exceptional burden on the Office. As the technical feature linking the members do not constitute a special technical feature as defined by PCT Rule 13.2, particularly since each of the embodiments does not share a substantially common structural feature or function, the requirement for unity of invention is not fulfilled.

Applicant is required to elect a single named embodiment as listed in the cited claims to which the claims shall be restricted. The reply must also identify the claims readable on the elected embodiments, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

See Restriction Requirement mailed March 29, 2007, pages 5-6.

Under the unity of invention standard as set forth in 37 C.F.R. § 1.475(a), the requirement of unity of invention is fulfilled when there is a technical relationship among the claimed subject matter involving a corresponding special technical feature. The expression "special technical features" means a technical feature that defines a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. Applicants respectfully submit that, when considered as a whole, each of claims 15-24 and 26-28, has a common special technical feature over the prior art. The special technical feature is a eucaryotic cell that includes a genetic sequence encoding a non-native antidote molecule to a poison protein from a poison antidote group, the poison protein being encoded by nucleotide sequence under control of an inducible operator/promoter that is incorporated into the genome of the cell. Each claim recites this technical feature. The Examiner has made no argument that this unifying technical feature does not define a contribution over the prior art. The Examiner's argument for restriction rather seems to be a mixture of the rules for restricting independent and distinct subject matter, the USPTO policy related to nucleotide and amino acid sequence searching, and the rules for restriction based on patentably distinct species all weaved together using the vocabulary found in the rules related to unity of invention requirement. As such, Applicants submit that the Examiner has failed to provide any appropriate reason under the unity of invention standard as to why the claimed subject matter should be restricted as set forth in section 3 of the Restriction Requirement.

In view of the above-described special technical feature, which is common to each of the elected claims, and the lack of any showing that this special technical feature does not make a contribution over the prior art, Applicants request that the Examiner withdraw the requirements for restriction as set out in section 3 of the Restriction Requirement.

In addition to the foregoing arguments, Applicants would like to point out that the poison proteins recited in claim 18, while not being obvious variants of each other, are related by both phylogenetically and by their mode of action. In particular, these proteins and their corresponding antidotes all form a group of procaryotic proteins referred to a plasmid addiction systems. The relationship among the proteins of plasmid addiction systems is described in the

art. For the Examiner's convenience, Applicants submit herewith an Information Disclosure Statement containing references, which describe the structural and functional relationship between the proteins of plasmid addition systems (see particularly, Gerdes et al. (2007) *Current Opinions in Microbiology* **10**:117-124; Anantharaman et al. (2003) *Genome Biology* **4**:R81.1-15; and Schmidt et al. (2007) *J. Mol. Biol.* - electronic publication, each of these references being provided in the IDS filed herewith).

Finally, to bring the claims into better conformance with US practice, Applicants have amended claims 15, 18, 24, 27 and 28 to remove conditional and alternative language, which the Examiner has alleged gives rise to lack of unity. If the Examiner believes that the claims as currently written still lack unity, he is invited to provide an explanation why they do not form a single inventive concept under 37 C.F.R. § 1.475.

Concluding remarks

Applicants have presented a generic claim, independent claim 15, that includes all of the embodiments set forth in each of the dependent claims. The Examiner has not characterized these embodiments as patentably distinct species, but rather, insists that these embodiments are patentably distinct inventions that should be excluded from search and examination. Applicants can find no legal basis for such an exclusion. Applicants respectfully submit that they have a statutory right under 35 U.S.C. §112, second paragraph, to claim the subject matter they regard as their invention. Maintaining the restriction of the embodiments as set forth by the Examiner in section 3 of the Restriction Requirement issued March 29, 2007 is tantamount to refusing to examine that which the Applicants regard as their invention. Accordingly, Applicants respectfully request rejoinder of these embodiments.

CONCLUSION

Applicants submit that the Examiner's grouping of inventions is arbitrary and that the Examiner's assertion that the embodiments set forth in section 3 of the Restriction Requirement issued March 29, 2007 should be excluded from search and examination is without logical or legal justification. Accordingly, Applicants respectfully request that the Commissioner overrule the Examiner's restriction requirement.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: June 10, 2008

By: _____

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